

REMARKS

Claims 1-95 were pending, claims 1-59 were withdrawn. Claims 60-95 were rejected. After entry of the amendments and remarks herein, claims 60-141 are pending. Claims 1-59 are herein canceled. Claims 60, 67, 75, 86-90 are herein amended. New claims 96-141 are herein added.

Amendments to the claims are made to more specifically point out and distinctly claim the subject matter regarded as invention. Such amendments should in no way be construed as acquiescence to any of the Examiner's rejections and were made solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

No new matter has been added by virtue of the amendments, support being found throughout the specification and claims as originally filed. Reconsideration is requested, at least for the reasons discussed herein.

Interview Summary

Applicants thank the Examiners Gough and Gitomer for the telephonic interview of August 7, 2008, which was helpful to clarify the bases for the Examiner's rejection of the instant claims under 35 U.S.C. § 112, first paragraph. During the interview Applicants explained the claimed invention to Examiners Gough and Gitomer. It was agreed that amending the claims to include additional method steps may clarify the invention for the Examiners. Applicants have herein amended the claims and introduced new claims which more clearly recite distinct method steps. Further, Applicants herein include arguments in support of the patentability under 35 U.S.C. § 112, §102 and §103 of the original claims, amended claims and new claims.

Rejection of the claims under 35 U.S.C. §112, first paragraph, written description

Claims 60, 67, 75, 86 and the claims dependent thereon (61-66, 68-74, 76-85 and 87-95) are rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to

comply with the written description requirement. The Examiner alleges that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, has possession of the claimed invention. Specifically, the Examiner asserts that the specification does not describe how one sample to be separated into components can differ in the amount of female vs. male cells over time and how a maximum in a curve is determined. As explained, the aliquots are taken from the sample at various times after collection, separation of female from male cells is performed and analysis by FISH is made. This is one way to determine the time needed to maximize the separation of female cells from male cells.

Thus, Applicants respectfully traverse the rejection. However, based on the Examiner interview on August 7, 2008, and in order to expedite prosecution of the present application, Applicants have amended independent claims 60, 67, 75, 86 to clearly convey distinct method steps for performing some embodiments of the claimed invention. Further, new independent claims 103, 106, 116, 125 and 131 are added.

Claimed invention

Claim 60 is directed to a method for treating a specimen of semen containing sperm cells to increase the relative number of sperm cells of a preferred sex type. The method entails collecting a sample of semen, holding the semen after collection for a predetermined period of time, and after the predetermined period of time, separating the semen into two components; a first component having a higher number of sperm of the preferred sex type and a second component having a higher number of sperm of the non preferred sex type relative to sperm of the preferred sex type. The separation step is performed in a window of time that can be determined by locating a maximum (e.g., maximum percent of female cells) in a curve obtained by plotting the percent of female cells determined by FISH against the percent cells that are Koo positive for aliquots of a sample wherein separation is performed at varying times of incubation after collection, thereby determining the time at which the maximum percent female cells occurs. Furthermore, the claimed separation step begins no earlier than about one hour before the time of the maximum percent of female cells. Independent claims

67 and 75 are directed to similar methods which utilize a window of time that can be determined by locating a maximum (e.g., maximum percent of female cells) in a curve obtained by plotting the percent of female cells determined by FISH against the percent cells that are Koo positive for aliquots of a sample wherein separation is performed at varying times of incubation after collection, thereby determining the time at which the maximum percent female cells occurs and beginning the separation step no earlier than about one hour before the time of the maximum percent female cells.

Amended claim 86 is directed to a method of increasing the percentage of mammalian offspring of a predetermined sex. In the method the semen is first collected, cooled to a predetermined temperature and incubated for a predetermined amount of time. The sample is contacted with a cell binding agent to preferentially bind a selected population of cells. The selected cells and binding agent are then separated so as to provide a treated sample containing non selected cells. At least a portion of the treated sample is administered to the reproductive tract of a female mammal.

The predetermined amount of time for the incubating step is determined by a method in which a test specimen of semen is collected; a first portion of the test specimen is incubated at a constant temperature for a first incubation period; a second portion of the test specimen is incubated at a constant temperature for a second incubation period; contacting the first and second portions of the test specimen with a binding agent which binds the selected population of cells; and the first and second portions are separated into selected and non selected test specimens. The predetermined amount of time for incubating the semen is then determined by identifying which of the incubation time periods yielded the maximum percent of female cells in the non selected test specimen.

New claim 103 is directed to a method for determining the optimum time to incubate a sample of semen prior to contacting the sample with a binding agent in order to enrich for female sperm cells. The method includes the steps of: (a) collecting a test specimen of semen; (b) cooling the test specimen to a predetermined temperature; (c) incubating the test specimen at the predetermined temperature for a first incubation period; (d) contacting the test specimen with a Koo antibody at the end of the incubation period; (e) separating the test specimen into Koo bound and Koo unbound test specimens; (f) determining the percent of female sperm cells in the Koo unbound

test specimen; (g) repeating at least steps (c) through (f) for at least a second incubation period, and (h) determining the incubation period that results in enrichment for the maximum percent of female cells. The steps need not be performed in the exact recited order. For example, step (f) can be performed after step (g).

New claim 106 is directed to a method for determining the optimum time to incubate a sample of semen prior to contacting the sample with a binding agent in order to enrich for female sperm cells. The method includes, collecting a test specimen of semen; incubating the test specimen at a constant temperature for two or more different incubation periods; contacting the test specimen at the end of the two or more incubation periods with a binding agent which binds the selected population of cells; and separating the test specimen into selected and non selected test specimens. The predetermined amount of time for incubating the semen is then determined by identifying which of the two or more incubation time periods yielded the maximum percent of female cells in the non selected test specimen.

Support for the amendments to claims 75 and 86 and new claims 103 and 106 can be found throughout the application and claims as filed, including claim 75 and 86, paragraphs [0013] – [0021] and [0026] – [0030] and Examples 1 and 3 of the application as published.

New claim 125 is directed to a method for determining the optimum time at which to separate male and female sperm cells. In the method a test specimen is collected; cooled to a predetermined temperature; incubated at the predetermined temperature for two or more different incubation periods; and the percent of sperm cells exhibiting sticky patches in the samples at the two or more different incubation periods is determined. The optimum time for separating male and female sperm cells is then identified as being the incubation period which resulted in at least about 20% of the sperm cells exhibiting sticky patches.

Support for the amendments to claim 125 can be found throughout the application and claims as filed, including paragraphs [0013] – [0016] and [0021].

New claim 131 is directed to a method for separating a selected population of cells from a sample of semen. In the method the semen is first cooled to a predetermined temperature and incubated for a predetermined amount of time. The sample is contacted with a cell binding agent to preferentially bind a selected population

of cells. The selected cells and binding agent are then separated so as to provide a treated sample containing non selected cells.

The predetermined amount of time for the incubating step is determined by a method in which a test specimen of semen is collected; incubated at a constant temperature for two or more different incubation periods; contacted at the end of the two or more incubation periods with a binding agent which binds the selected population of cells; and separated into selected and non selected test specimens. The predetermined amount of time for incubating the semen is then determined by identifying which of the two or more incubation time periods yielded the maximum percent of female cells in the non selected test specimen. Support for claim 131 is found in claim 75 as filed and [0013] – [0021] and [0026] – [0030] and Examples 1 and 3 of the application as published.

The claimed invention satisfies the written description standard

The Examiner asserts that “[i]t is not described in the specification how one sample to be separated into two components can differ in the amount of female vs. male cells over time . . .” and that [a]pplicant appears to be claiming using the FISH analysis to track when more female sperm cells are present in a single sample, for which there is no scientific support . . .”

As discussed during the Examiner interview on August 7th, the Applicant is not asserting that an **unseparated** sample differs in the amount of female vs. male cells over time, although this may be possible, e.g., preferential cell death of female or male cells. Rather, the amounts (percentages) of female vs. male cells differs over time. When a **sample has been separated into a female cell component and a male cell component**; e.g., **a result of Y-bearing sperm's (male sperm's) ability to adhere to cell binding agents (e.g., H-Y binding agents, e.g., Koo antibody) in greater proportion than X-bearing sperm (female sperm) and the discovery that this difference is most pronounced at a particular time after collection.** Thus, this discovery allows for the **greater separation** of Y and X-bearing sperm when the separation procedure is performed at a time when the binding agent binds Y-bearing sperm in greater proportion than X-bearing sperm. This differential binding ability of Y-

vs. X- sperm is evident throughout the application as filed, and is specifically illustrated in Example 1 and the related data of Tables 1 & 2. Paragraph 13 of the publication explains this discovery:

We have discovered that there is a period of time, i.e., a sexing window, during **which Y-chromosome bearing sperm develop an ability to adhere or bind to cell binding agents in greater proportion than X-chromosome bearing sperm.** If the spermatozoa are treated with a cell binding agent in this window, Y-chromosome bearing sperm will adhere or bind preferentially to a cell binding agent whereas X-chromosome bearing sperm will remain preferentially in the fluid. Thus, **separating the cell binding agent with preferentially bound Y-chromosome bearing sperm will remove Y-chromosome bearing sperm preferentially leaving a higher percentage of X-chromosome bearing sperm, thereby biasing the remaining non bound sperm for producing female offspring when introduced into a suitable fertile mammal.** [Emphasis added]

The reason for Y-sperm's preferential binding to binding agents and, in particular, the change in this binding over time is not fully understood, but understanding how this change occurs is not necessary for patentability. The Federal Circuit has held that an inventor need not understand how his invention works (*Cross v. Iizuka*, 753 F.2d 1040, 224 U.S.P.Q. 739 (Fed. Cir. 1985), ". . . it is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests, nor is the inventor's theory or belief as to how his invention works a necessary element in the specification to satisfy the enablement requirement of 35 U.S.C. § 112." (at 741, footnote 3), citing *Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1570, 219 USPQ 1137, 1140 (Fed. Cir. 1983)). Nonetheless, while not being bound by theory, it is hypothesized that this change in binding (e.g., Koo antibody binding) over time may be the result of one or more of the following; increased expression of the Koo antibody's antigen post collection, continued development of the "sticky patch" (See paragraph 28 of the publication), unmasking of a binding antigen on the cell, e.g., through the loss of another molecule which masks the binding antigen. Thus, the application clearly teaches how the ratio of male to female sperm cells can change in sperm samples that have been fractionated by binding agents at various times after a post collection incubation step.

The Examiner stated that the specification does not describe how a maximum time is determined. Applicants respectfully disagree. The application fully describes how a maximum of time is determined. In particular this is evident in Examples 1 and 3 and the detailed protocols starting at paragraph 86 of the publication and continuing to paragraph 173.

The maximum in time can be determined by several methods. For example, paragraph 15 of the publication teaches that the maximum in time occurs when:

The window opens when a sufficient number of sperm cells exhibit the sticky patches so that separation preferentially removes sufficient Y-chromosome bearing sperm so that the remaining non bound sperm is biased to a desired level with X-chromosome bearing sperm. **The window closes when a sufficient number of sperm cells exhibit the sticky patches so that separation can no longer provide the desired biased level.** [Emphasis added]

Furthermore, paragraph [0016] teaches that the maximum in time can be determined by Koo staining:

In certain preferred embodiments of the invention, the window opens with the appearance of the sticky patches on at least about 20% of the sperm cells in the semen, preferably at least about 25%, and more preferably at least about 30%, as determined by labeling the sperm with Koo antibody. The window closes when more than more than 40% of the sperm cells have sticky patches, preferably more than 35%, as determined by labeling the sperm with Koo antibody.

Another means by which to determine a maximum is by determining the time point when the maximum percent of female cells is obtained in a test sample that has been separated into unbound and bound fractions. This identified maximum for female sperm cell enrichment is then later used for the actual enrichment of female sperm cells. This method is detailed in new claim 103, which is described above.

In a preferred embodiment, the maximum is identified by contacting the semen specimens that have been incubated at various times post collection at a constant temperature with a Koo antibody, which preferentially binds the Y-sperm, allowing the separation of the bound sperm from the non-bound sperm which remains in the fluid. FISH may then be performed on the unbound sperm

in the fluid (e.g., Table 2) to determine the percent of female sperm cells. When these results are plotted, it is readily apparent that, during a specific window/period of time, the **separated unbound sample** will exhibit a significantly higher percent of X-sperm (female sperm) than Y-sperm (male sperm). This maximum percent of X-sperm is readily apparent on the Koo vs. FISH graphs of Figs. 2-4 which illustrate the data in Table 1 (percent of cells ICC positive with Koo) plotted against the data of Table 2 (percent of female cells in the fluid after separation as assayed by FISH). As observable in each graph there is a point at which the maximum number of X-sperm remain in the **separated unbound fraction** as was determined by FISH. **It is the incubation time point which corresponds to the separated unbound fraction containing the maximum number of X-sperm cells at which performing the separation protocol is optimal in order to enrich for X-sperm.**

The Examiner also asserts that, "it appears as if the FISH analysis is merely a measure of time and temperature compared to the staining process, i.e., the optimum time and temperature at which the ICC positive cells are stained, not a determination of when more female sperm exist in a sample." This is incorrect.

All Koo and FISH staining were performed under **consistent time and temperature conditions** (See Example 1). For example, **there is no difference in the conditions (temperature or time) in which the Koo staining protocol was performed on the sample taken at either the two hours post collection or 12 hours post collection times (See Tables 1 and 2).** The only variable is the time at which the semen specimen is incubated (prior to contacting with the binding agent or staining agent) at a constant temperature post collection ***but before staining.***

In light of the above, it is clear the claims are fully supported by the application as filed. Thus, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 60, 67, 75, 86 and the claims dependent

thereon (61-66, 68-74, 76-85 and 87-95), under 35 U.S.C. §112, first paragraph for alleged lack of written description.

Rejection of the claims under 35 U.S.C. §112, first paragraph enablement

Claims 60, 67, 75, 86 and the claims dependent thereon (61-66, 68-74, 76-85 and 87-95) are rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the enablement requirement. The Examiner alleges that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. This rejection is very much interrelated with the with the written description rejection discussed above.

Applicants respectfully traverse the rejection.

First, Applicants note that claims 60, 67, 75 and 86 is herein amended to clearly convey discrete method steps for performing some embodiments of the claimed invention. Further, new independent claims 103, 106, 116, 125 and 131 contain clear method steps. The arguments presented above for the written description rejections address most of the issues the Examiner raised with respect to enablement. Thus, rather than reargue the arguments presented above Applicants direct the Examiner to the above arguments which support both written description and enablement of the claims. Only those issues raised in the enablement rejection which are not fully addressed above will be discussed below.

The Examiner asserts:

Further, applicants specification, examples, Tables, etc only practice the invention with the female cells being the preferred sex type, not at all enabling one to obtain a preferred **male** sample. Moreover, the examples provided do not support obtaining a preferred male sex type in applicants claimed method. Thus, in view of the lack of any specific guidance with respect to how to obtain a male preferred sex type using applicant method, one skilled in the art would expect a trial and error process to determine how such a preference can be analyzed using such method and how determining such would apply to the as disclosed application, and would further have to determine through undue experimentation,

without guidance from the specification, how to obtain a male population using the steps and methods of the invention.

Applicants respectfully disagree.

Based on the teachings in the application and what was known in the art, the application clearly enables one skilled in the art to practice the claimed invention to obtain a preferred male sample. As discussed above, the sperm cell sample can be separated into two fractions (bound and unbound) by utilizing the cell binding agents. In a preferred embodiment, the bound cell fraction preferentially includes Y-sperm and the liquid unbound cell fraction preferentially includes X-sperm. Thus, the application teaches the preferential isolation of both male (Y-sperm) and female cells (X-sperm). In selecting for a preferred male phenotype the binding agent bound sperm is selected for in vitro fertilization rather than the unbound sperm (female). Thus, the techniques for the preferential selection of male vs. female sperm are essentially identical except that the male sperm are obtained from the bound fraction.

The method for obtaining a preferred male sperm fraction is taught throughout the application, including, for example, paragraph 22 of the publication: "[t]he desired or preferred sex can vary with application. Also, the selected sperm cells can be either the bound cells or the non bound cells, depending on the application."

Furthermore, paragraph 64 states:

bound sperm cells also can be recovered, thus, providing separation and isolation of the two populations of spermatozoa (i.e., X-and Y-bearing sperm). Recovery of the magnetic component is easily performed by removing the separation container from the magnetic separator and then draining the container. **Reversal of the binding is accomplished in the same manner as in certain types of chromatography or antibody-antigen reactions.** [Emphasis added]

Thus, it is clear that, based on the specification and what was known in the art at the time of filing, one of ordinary skill could practice the claimed invention without undue experimentation. In light of the above, Applicants respectfully request the Examiner reconsider and withdraw the rejection of claims 60, 67, 75, 86 and the claims dependent thereon (61-66, 68-74, 76-85 and 87-95) under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the enablement requirement.

Rejection of the claims under 35 U.S.C. §112, second paragraph

Claims 60, 67, 75, 86 and the claims dependent thereon (61-66, 68-74, 76-85 and 87-95) are rejected under 35 U.S.C. 112, second paragraph, for allegedly being indefinite. The Examiner alleges that it is unclear how a sperm sample can produce more female than male sperm, what the curve is, how the window of time is determined, whether applicant is separating/sorting by FISH or by a different method and whether or not FISH is necessarily required by the method.

Applicants respectfully disagree with the rejection. Applicants note that the claims are herein amended to more clearly recite method steps.

It is believed that the claim amendments and Applicants' response to the written description rejection has clarified these issues, and specifically refer the Examiner to the arguments presented therein. In light of the above, Applicants respectfully request withdrawal of the rejection of claims 60, 67, 75, 86 and the claims dependent thereon (61-66, 68-74, 76-85 and 87-95) for alleged indefiniteness.

Rejection of the claims under 35 U.S.C. §102

As the Examiner is well aware in order to anticipate a claim, each and every element of the claim must be found in a single reference. This is discussed in the Manual of Patent Examining Procedure § 2131:

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). "The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

Claims 60, 61, 63 and 75 are rejected under 35 U.S.C. 102(b) over Sills et al. (American Journal of Reproductive Immunology, vol. 40, 1998; "Sills"). Applicants traverse the rejection. Applicants note that independent claims 60 and 75 are herein amended to clearly convey discrete method steps for performing some embodiments of the claimed invention.

First, Sills fails to teach or suggest holding or incubating semen for a predetermined time before separating female cells from male cells.

Further, Sills concludes that:

[t]he expression of H-Y antigen has a slightly higher frequency in human sperm containing the Y-chromosome, but its expression among X-chromosome-bearing sperm also is considerable. **Current immunological techniques relying on this antigen are unlikely to effect sex selection of human sperm. [Emphasis added]**

Thus, Sills **fails** to teach or suggest a method for treating a specimen of semen containing sperm cells to increase the relative number of sperm cells of a preferred sex type in a treated specimen to increase the potential for conceiving an offspring of the preferred sex, as claimed herein. In fact Sills et al. teaches away from the claimed invention by stating, "[c]urrent immunological techniques relying on this antigen [H-Y antigen] are unlikely to effect sex selection of human sperm." The Koo antibody utilized in some methods of the claimed invention is specific for the H-Y antigen. Thus, Sills et al. teaches away from using the H-Y antigen and thus the Koo antibody in sex selection. It was not until the present invention that it was shown that a more meaningful enrichment of female sperm cells can occur with a negative selection method based on binding to the H-Y antigen.

Sills also **fails** to teach or suggest a method that includes:

separating the semen into two components comprising a first component having a higher number of sperm of the preferred sex type than sperm of a non preferred sex type and a second component having a higher number of sperm

of the non preferred sex type relative to sperm of the preferred sex type,

as claimed herein.

Further, Sills **fails** to teach or suggest a method

wherein the separating step is performed in a window of time that can be determined by locating a maximum in the curve obtained by plotting percent female cells determined by FISH against percent Koo positive cells for aliquots of another semen sample, the aliquots being taken at various times after collection, determining the time at which the maximum percent female cells occurs, and determining the period of time for holding the semen after collection before and beginning the separation step to provide a time no earlier than about one hour before the time of the maximum percent female cells as determined by FISH.

Thus, it is not seen how the presently claimed invention is anticipated by Sills. Further, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Sills.

Claims 60-62, 67-69, 82-83, 86-91 and 93 are rejected under 35 U.S.C. 102(b) over Benjamin (US 6153373). Applicants traverse the rejection. Independent claims 60, 67, 75 and 86 are herein amended.

Although Benjamin '373 describes a method for increasing the percentage of mammalian offspring of either sex by contacting a sperm sample with an antibody specific to a selected spermatozoa type. Benjamin **fails** to teach or suggest that a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex, the increase being compared to separation performed outside the window.

Further, Benjamin fails to teach or suggest:

incubating the semen for a predetermined amount of time at the predetermined temperature, wherein the predetermined amount of time can be determined by a method comprising the steps of: collecting a test specimen of semen; incubating the test specimen at a constant temperature for two or more different incubation periods; contacting the test specimen at the end of the two or more incubation periods with a binding agent which binds the selected population of cells; separating the test specimen into selected and non selected test specimens, and determining which of the two or more incubation time periods yielded the maximum percent female cells in the non selected test specimens, thereby identifying the predetermined amount of time for incubating the semen; [Claim 86]

Indeed, Benjamin '373 does not even suggest that such a window can exist. Present Applicants have discovered the existence of a time period for the preferential binding of male sperm to binding agents and how to use it for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex.

Thus, it is not seen how the presently claimed invention is anticipated by Benjamin '373. Further, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Benjamin '373.

Claims 60-62, 67-69, 82-83, 86-91 and 93 are rejected under 35 U.S.C. 102(a) and (e) over Benjamin (US2003/0068654A1). Applicants traverse the rejection. Independent claims 60, 67, 75 and 86 are herein amended.

Although Benjamin '654 describes a method for increasing the percentage of mammalian offspring of either sex by contacting a sperm sample with an antibody specific to a selected spermatozoa type, Benjamin *fails* to teach or suggest that a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex. Indeed, Benjamin '654 does not even suggest that such a window can exist. Present Applicants have discovered the existence of this window and how to use it for performing the separation to obtain the desired increase in the percentage of mammalian offspring of either sex.

Further, Bajamin '654 fails to teach or suggest:

incubating the semen for a predetermined amount of time at the predetermined temperature, wherein the predetermined amount of time can be determined by a method comprising the steps of: collecting a test specimen of semen; incubating the test specimen at a constant temperature for two or more different incubation periods; contacting the test specimen at the end of the two or more incubation periods with a binding agent which binds the selected population of cells; separating the test specimen into selected and non selected test specimens, and determining which of the two or more incubation time periods yielded the maximum percent female cells in the non selected test specimens, thereby identifying the predetermined amount of time for incubating the semen; [Claim 86]

Indeed, Benjamin '654 does not even suggest that such a window can exist. Present Applicants have discovered the existence of a time period for the preferential binding of male sperm to binding agents and how to use it for performing the separation to obtain the desired increase in the percentage of mammalian offspring of either sex.

Thus, it is not seen how the presently claimed invention is anticipated by Benjamin '654. Further, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Benjamin '654.

Claims 60-62, 67-69, 82-83, 86-91 and 93 are rejected under 35 U.S.C. 102(a) and (e) over Benjamin (6489092). Applicants traverse the rejection. Independent claims 60, 67, 75 and 86 are herein amended.

Although Benjamin '092 describes a method for increasing the percentage of mammalian offspring of either sex by contacting a sperm sample with an antibody specific to a selected spermatozoa type, Benjamin **fails** to teach or suggest that a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex. Indeed, Benjamin '092 does not even suggest that such a window can exist.

Further, Benjamin '092 fails to teach or suggest:

incubating the semen for a predetermined amount of time at the predetermined temperature, wherein the predetermined amount of time can be determined by a method comprising the steps of: collecting a test specimen of semen; incubating the test specimen at a constant temperature for two or more different incubation periods; contacting the test specimen at the end of the two or more incubation periods with a binding agent which binds the selected population of cells; separating the test specimen into selected and non selected test specimens, and determining which of the two or more incubation time periods yielded the maximum percent female cells in the non selected test specimens, thereby identifying the predetermined amount of time for incubating the semen; [Claims 75 and 86]

Indeed, Benjamin '092 does not even suggest that such a window can exist. Present Applicants have discovered the existence of time period for the preferential binding of male sperm to binding agents and how to use it for performing the separation to obtain the desired increase in the percentage of mammalian offspring of either sex.

Thus, it is not seen how the presently claimed invention is anticipated by Benjamin '092. Further, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Benjamin '092.

Claims 60-63, 67-70 and 75 are rejected under 35 U.S.C. 102(b) over Blecher et al (US2001/0041348 A1; "Blecher"). Applicants respectfully traverse the rejection. Claims 60, 67 and 75 are herein amended.

Although Blecher describes a method for separating semen into male and female determining sperm with antibodies bound to carriers, such as beads, specific for sex-chromosome molecules, Blecher *fails* to teach or suggest that a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex. Indeed, Blecher does not even suggest that such a window can exist. Present Applicants have discovered the existence of this window and how to use it for performing the separation to obtain the desired increase in the percentage of mammalian offspring of either sex.

Thus, it is not seen how the presently claimed invention is anticipated by Blecher. Further, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Blecher.

Claims 60-62, 67-69, 75 and 82 are rejected under 35 U.S.C. 102(b) as being anticipated by Zavos et al. (4999283). Applicants traverse the rejection. Independent claims 60, 67 and 75 are herein amended.

Zavos et al. *fails* to teach or suggest determining a window of time after ejaculation and using the identified window of time for performing the separation step to obtain an increase in the percentage of mammalian offspring of either sex. Indeed, Zavos et al does not even suggest that such a window can exist. Present Applicants have discovered the existence of this window and how to use it for performing the separation to obtain the desired increase in the percentage of mammalian offspring of either sex.

Thus, it is not seen how the presently claimed invention is anticipated by Zavos et al. Further, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Zavos et al.

Claims 60-62, 67-69, 73 and 74 are rejected under 35 U.S.C. 102(b) as being anticipated by Van den Bovenkamp (3687806). Applicants traverse the rejection. Independent claims 60 and 67 are herein amended. Van den Bovenkamp *fails* to teach or suggest determining a window of time after ejaculation and using the identified window of time for performing the separation step to obtain an increase in the percentage of mammalian offspring of either sex. Indeed, Van den Bovenkamp does not even suggest that such a window can exist. Present Applicants have discovered the existence of this window and how to use it for performing the separation to obtain the desired increase in the percentage of mammalian offspring of either sex.

Thus, it is not seen how the presently claimed invention is anticipated by Van den Bovenkamp. Further, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Van den Bovenkamp.

Claims 60-63, 67-70, 75-80, 82-83, 86-91 and 93 are rejected under 35 U.S.C. §103(a) over Benjamin '654A1 or Benjamin '373 or Benjamin '092 in view of Sills (AJRI, vol. 40, 1998). Independent claims 60, 67, 75 and 86 are herein amended. The Examiner states that it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used FISH in analyzing the percentage of male vs. female sperm cells in a sample. Applicants agree. However, that is not the presently claimed invention.

The present invention provides, in part, a method for identifying a particular incubation period which is followed by a separation procedure of the semen sample into male-rich and female-rich components. The specification describes that the period of time can be determined by using FISH with Koo positive cells to determine the time when particular sex type sperm cells are at a maximum and uses that time to determine the window for obtaining optimal separation of male and female sperm cells. None of the cited prior art teach or suggest such a period of time. Not one of Benjamin '654 or Benjamin '373 or Benjamin '092 or Sills, or their combination, teach or suggest a method for identifying a period of time after ejaculation for performing a separation procedure to obtain an increase in the percentage of mammalian offspring of either sex.

Thus, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Benjamin '654 or Benjamin '373 or Benjamin '092 or Sills, or any combination of them.

Claims 60-63, 67-70 and 75 are rejected under 35 U.S.C. §103(a) over Blecher '348 in view of Sills. Applicants traverse the rejection. Independent claims 60, 67 and 75 are herein amended.

The present invention provides a window for performing a separation of the semen sample into male-rich and female-rich components. The specification describes that the window can be determined by using FISH with Koo positive cells to determine the time when particular sex type sperm cells are at a maximum and uses that time to determine the window. None of the cited prior art teach or suggest such a window of time. Neither Blecher nor Sills, nor their combination, teach or suggest a window of

time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex. The present invention uses a window for performing a separation into of the semen sample into male-rich and female-rich components. None of the cited prior art teach or suggest such a window of time.

Thus, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Blecher or Sills, or any combination of them.

Claims 60-62, 67-69, 75 and 82 are rejected under 35 U.S.C. §103(a) over Zavos et al. (US 4999283; "Zavos") in view of Sills. Independent claims 60, 67 and 75 are herein amended. The present invention provides an optimized time (e.g., window) for performing a separation of the semen sample into male-rich and female-rich components. The specification describes that the window can be determined by using FISH with Koo positive cells to determine the time when particular sex type sperm cells are at a maximum and uses that time to determine the window. None of the cited prior art teach or suggest such a window of time. Neither Zavos nor Sills, nor their combination, teach or suggest a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex. The present invention uses a window for performing a separation into of the semen sample into male-rich and female-rich components. None of the cited prior art teach or suggest such a window of time.

Thus, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Zavos or Sills, or any combination of them.

Claims 60-62, 67-69, 73 and 74 are rejected under 35 U.S.C. §103(a) over Van den Bovenkamp (US 3687806) in view of Sills. Independent claims 60 and 67 are herein amended. The present invention provides a window for performing a separation of the semen sample into male-rich and female-rich components. The specification describes that the window can be determined by using FISH with Koo positive cells to

determine the time when particular sex type sperm cells are at a maximum and uses that time to determine the window. None of the cited prior art teach or suggest such a window of time. Neither Van den Bovenkamp nor Sills, nor their combination, teach or suggest a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex. The present invention uses a window for performing a separation into of the semen sample into male-rich and female-rich components. None of the cited prior art teach or suggest such a window of time.

Thus, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Van den Bovenkamp or Sills, or any combination of them.

Claims 60-63, 67-70, 75-80, 82-83, 86-91 and 93 are rejected under 35 U.S.C. §103(a) over Benjamin '654A1 or Benjamin '373 or Benjamin '092 in view of Johnson (Reprod. Fertil. 1995). Independent claims 60, 67, 75 and 86 are herein amended. The Examiner states that it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used FISH in analyzing the percentage of male vs. female sperm cells in a sample. Applicants agree. However, that is not the presently claimed invention.

The present invention provides a method for utilizing an optimized period of time (e.g., window of time) in which separating a semen sample into male-rich and female-rich components is most effective. The specification describes that the window can be determined by using FISH with Koo positive cells to determine the time when particular sex type sperm cells are at a maximum and uses that time to determine the window. None of the cited prior art teach or suggest such a window of time. Not one of Benjamin '654A1 or Benjamin '373 or Benjamin '092 or Johnson, or their combination, teach or suggest a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex.

Thus, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Benjamin '654A1 or Benjamin '373 or Benjamin '092 or Johnson, or any combination of them.

Claims 60-63, 67-70 and 75 are rejected under 35 U.S.C. §103(a) over Belcher '348A1 in view of Johnson. Independent claims 60, 67 and 75 are herein amended. The present invention provides a method for utilizing an optimized period of time (e.g., window of time) in which separating a semen sample into male-rich and female-rich components is most effective. The specification describes that the window can be determined by using FISH with Koo positive cells to determine the time when particular sex type sperm cells are at a maximum and uses that time to determine the window. None of the cited prior art teach or suggest such a window of time. Neither Blecher nor Johnson, nor their combination, teach or suggest a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex. The present invention uses a window for performing a separation into of the semen sample into male-rich and female-rich components. None of the cited prior art teach or suggest such a window of time.

Thus, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Blecher or Johnson, or any combination of them.

Claims 60-62, 67-69, 75 and 82 are rejected under 35 U.S.C. §103(a) over Zavos in view of Johnson. Independent claims 60, 67 and 75 are herein amended. The present invention provides a method utilizing an optimized period of time (e.g., window of time) in which separating a semen sample into male-rich and female-rich components is most effective. The specification describes that the window can be determined by using FISH with Koo positive cells to determine the time when particular sex type sperm cells are at a maximum and uses that time to determine the window. None of the cited prior art teach or suggest such a window of time. Neither Zavos nor Johnson, nor their combination, teach or suggest a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of

mammalian offspring of either sex. The present invention uses a window for performing a separation into of the semen sample into male-rich and female-rich components. None of the cited prior art teach or suggest such a window of time.

Thus, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Zavos or Johnson, or any combination of them.

Claims 60-62, 67-69, 73 and 74 are rejected under 35 U.S.C. §103(a) over Van den Bovenkamp in view of Johnson. Independent claims 60 and 67 are herein amended. The present invention provides a window for performing a separation of the semen sample into male-rich and female-rich components. The specification describes that the window can be determined by using FISH with Koo positive cells to determine the time when particular sex type sperm cells are at a maximum and uses that time to determine the window. None of the cited prior art teach or suggest such a window of time. Neither Van den Bovenkamp nor Johnson, nor their combination, teach or suggest a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex. The present invention uses a window for performing a separation into of the semen sample into male-rich and female-rich components. None of the cited prior art teach or suggest such a window of time.

Claims 60-63, 67-70, 75-80, 82-83, 86-91 and 93 are rejected under 35 U.S.C. §103(a) over Benjamin '654A1 or Benjamin '373 or Benjamin '092 in view of Spaulding (US 5021244). Independent claims 60, 67, 75 and 86 are herein amended. The Examiner states that it would have been obvious to one of ordinary skill in the art at the time the invention to cool the semen after collection. However, embodiments of the presently claimed invention are more than merely cooling the semen.

The present invention provides a method utilizing an optimized period of time (e.g., window of time) in which separating a semen sample into male-rich and female-rich components is most effective. The specification describes that the window can be determined by using FISH with Koo positive cells to determine the time when particular

sex type sperm cells are at a maximum and uses that time to determine the window. None of the cited prior art teach or suggest such a *window* of time. Not one of Benjamin '654A1 or Benjamin '373 or Benjamin '092 or Spaulding, or their combination, teach or suggest a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex.

Thus, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Benjamin '654A1 or Benjamin '373 or Benjamin '092 or Spaulding, or any combination of them.

Claims 60-63, 67-70 and 75 are rejected under 35 U.S.C. §103(a) over Belcher '348A1 in view of Spaulding. Independent claims 60, 67 and 75 are herein amended. The present invention provides a method utilizing an optimized period of time (e.g., window of time) in which separating a semen sample into male-rich and female-rich components is most effective. The specification describes that the window can be determined by using FISH with Koo positive cells to determine the time when particular sex type sperm cells are at a maximum and uses that time to determine the window. None of the cited prior art teach or suggest such a window of time. Neither Blecher nor Spaulding, nor their combination, teach or suggest a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex. The present invention uses a window for performing a separation into of the semen sample into male-rich and female-rich components. None of the cited prior art teach or suggest such a window of time.

Thus, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Blecher or Spaulding, or any combination of them.

Claims 60-62, 67-69, 75 and 82 are rejected under 35 U.S.C. §103(a) over Zavos in view of Spaulding. Independent claims 60, 67 and 75 are herein amended. The present invention provides a method utilizing an optimized period of time (e.g., window of time) in which separating a semen sample into male-rich and female-rich

components is most effective. The specification describes that the window can be determined by using FISH with Koo positive cells to determine the time when particular sex type sperm cells are at a maximum and uses that time to determine the window. None of the cited prior art teach or suggest such a window of time. Neither Zavos nor Spaulding, nor their combination, teach or suggest a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex. The present invention provides a window for performing a separation into of the semen sample into male-rich and female-rich components. None of the cited prior art teach or suggest such a window of time.

Thus, it is not seen how the presently claimed invention would have been obvious to one of ordinary skill in the art in view of Zavos or Spaulding, or any combination of them.

Claims 60- 62, 67-69, 73 and 74 are rejected under 35 U.S.C. §103(a) over Van den Bovenkamp in view of Spaulding. Independent claims 60 and 67 are herein amended. The present invention provides a window for separating the semen sample into male-rich and female-rich components. The specification describes that the window can be determined by using FISH with Koo positive cells to determine the time when particular sex type sperm cells are at a maximum and uses that time to determine the window. None of the cited prior art teach or suggest such a window of time. Neither Van den Bovenkamp nor Spaulding, nor their combination, teach or suggest a window of time after ejaculation can be determined for performing the separation to obtain an increase in the percentage of mammalian offspring of either sex. The present invention uses a window for performing a separation into of the semen sample into male-rich and female-rich components. None of the cited prior art teach or suggest such a window of time.

SUMMARY

In view of the above amendment, Applicants believe the pending application is in condition for allowance, and such action is respectfully requested.

If for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, the Commissioner is hereby authorized and requested to charge Deposit Account No. **04-1105**.

Dated: 11/26/08

Respectfully submitted,

By Jeffrey L. Kopacz/

Jeffrey L. Kopacz, Esq.

Registration No.: 54,744

EDWARDS ANGELL PALMER & DODGE

LLP

P.O. Box 55874

Boston, Massachusetts 02205

(617) 439-4444

Attorneys/Agents For Applicant